UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,425	11/13/2003	Frank D. Lee	EPT-001C1	9956

51414 7590 12/08/2006

GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
EXCHANGE PLACE
BOSTON, MA 02109-2881

EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,425	LEE ET AL.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35 and 126-132* is/are pending in the application.

4a) Of the above claim(s) *11,15,26-30 and 128* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-14,16-25,31-35,126,127 and 129-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3 pages (10/6/06)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments and amendments, filed September 29, 2006, have been fully considered and they are deemed to be persuasive in-part. The following rejections and/or objections are reiterated and modified to address the amended claims. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1-10, 12-14, 16-25, 31-35, 126, 127, and 129-132 are under examination.

Claims 11, 15, 26-30, and 128 are withdrawn as being directed toward an unelected invention. Instant claim 128 is drawn to a stainable dye, not the elected fluorescent label.

Claims 36-125 are cancelled (claims 37-125 are drawn to an unelected invention).

Information Disclosure Statement

2. Items C32, C33, and C34 listed on the Information Disclosure Statement filed October 6, 2006 has not been considered because they are not published documents.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-3, 7-10, 12-14, 16-25, 31- 35, 126, 127,129, and 130-132 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katz (US 2002/0137119 A1) in view of Gembitsky et al. (US 2005/0153298).

The instant claims are drawn to method of detecting the presence of post-translational modification on a sample that include the steps of identifying potential post-translational modification sites and a proteome epitope tag on the fragments of a protein from a sample, generating a capture agent that binds to the proteome epitope tag, subjecting the sample to a treatment to solublize the fragments, and detecting the presence or absence of a post-translational modification. In addition, the instant claims also include steps of using a secondary capture agent specific for post-translational modification. It is noted that the term "Proteome Epitope Tag" is not specifically defined in the specification, thus this phrase has been interpreted to mean epitopes that identify a protein.

Regarding claim 1, Katz teaches a method that computationally identifies amino acid sequences from a sample of proteins wherein each fragment contains a unique proteome epitope tag (i.e., unique antigen) (page 2, paragraphs 0020-0022; page 4, paragraph 0062; page 5, paragraph 0082) and a post-translational modification site (page 5, paragraph 0076; page 6, paragraphs 0091, 0093); generating a capture agents that bind to the PET (page 4, paragraph 0068) which may be immobilized to a support (page 8, paragraph 0140); subjecting the sample to render the fragment soluble in solution (page 8, paragraph 0137-0139); detecting the presence or absence of post-translational modification (page 6, paragraph 0091).

Although Katz teaches identifying post-translational modifications (page 5, paragraph 0076; page 6, paragraphs 0091, 0093), Katz does not specifically teach using a secondary capture agent.

Regarding claims 23-25, 127, and 130-132, Gembitsky et al. teach using a fluorescent-labeled secondary capture agent (full-length antibody) specific for phosphorylated tyrosine (page 3, paragraphs 0033, 0034; page 4, paragraphs 0039, 0040; page 5, paragraph 0046; page 7, paragraph 0074).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Katz with Gembitsky et al. to gain the advantage of high throughput analysis of cellular protein modifications. Katz teaches creating protein fragments and then binding the fragments to immobilized antibodies (page 8, paragraph 0140). Katz also teaches detecting the presence or absence of post-translational modifications (page 5, paragraph 0076; page 6, paragraphs 0091, 0093). Katz teaches

using well-known techniques for detecting post-translational modifications. However Gembitsky et al. teach that these well-known techniques lack expression profiling that allows parallel quantitation of all proteins expressed in a cell or tissue that analyzes the type, degree and timing of dynamic post-translational protein modifications (page 2, paragraph 0013). Gembitsky et al. teach that their method fulfills this need and allows the practitioner to perform a high throughput and quantitative method of comparative analysis of post-translational protein modifications (page 2, paragraph 0016). Thus one of ordinary skill in the art would be motivated to combine the methods of Katz with Gembitsky et al. to gain the advantages taught by Gembitsky et al.

Regarding claims 2, 3 and 126, Katz teaches wherein the post-translational modification is phosphorylation is on tyrosine (page 6, paragraph 0091).

Regarding claim 7, Katz teaches analyzing amino acid sequences in terms of solubility (page 5, paragraph 0076).

Regarding claim 8, Katz teaches that the fragments are 5-12 amino acids in length (page 6, paragraph 0094).

Regarding claim 9, 10 and 129, Katz teaches that the capture agents may be full-length antibodies (proteins) (page 7, paragraphs 0126-0129).

Regarding claims 12 and 16, Katz teaches wherein the treatment is by a protease or chemical agent (page 3, paragraphs 0043-0044; page 8, paragraph 0138).

Regarding claims 13 and 14, Katz teaches denaturizing using chemical or thermo means (page 12, paragraph 0171; page 13, paragraph 0178).

Regarding claims 17 and 18, Katz teaches that the sample may be obtained from a variety of sources (page 8, paragraph 0136; page 7, paragraph 0125; page 14, paragraph 0187).

Regarding claim 19, Katz teaches that a sample is produced by treatment of membrane bound proteins (page 9, paragraph 0157).

Regarding claims 20 and 21, Katz teaches where the post-translational modification is preserved and does not overlap with the PET (page 6, paragraph 0091-0093).

Regarding claim 22, Katz et al. teach optimizing the specificity of antibodies (page 4, paragraph 0058; page 7, paragraph 121-123, 130).

Regarding claim 31, Katz et al. teach identifying a fragment from a sample containing unrelated proteins (page 14, paragraph 0187-189).

Regarding claim 32, Katz teaches determining the amount of fragments bound to capture agents (page 8, paragraph 0143).

Regarding claim 33, Katz teaches where capture agents are produced by immunizing animals with the antigen with the PET sequence (page 7, paragraph 0125).

Regarding claim 34 and 35, Katz teaches labeling the protein fragments which would block the N or C-terminus of the PET sequence by a chemical group (page 13, paragraph 0175).

Response to Arguments

5. The Applicants have responded tot his rejection by stating that neither Katz or Gembitsky et al. teaches identifying fragments with a posttranslational modification site and a PET nor do they teach detecting on the fragment a post-translational modification with a secondary capture agent. The Examiner disagrees.

As stated above, Katz teaches identifying fragments with a post-translational modification site and a PET (page 2, paragraphs 0020-0022; page 4, paragraph 0062; page 5, paragraph 0082; page 5, paragraph 0076; page 6, paragraphs 0091-0093). Although Katz does prefer that the fragments do not have post-translational modification, he also specifically states, "peptide products which include post-translational modification, which indicate a biological activity of the polypeptide of interest can also be used by the present invention." (page 6, paragraph 0093). Thus Katz does teach the instant limitation.

The applicants also state that neither Katz or Gembitsky et al. teach detecting on the fragment a post-translational modification using a secondary capture agent. The Examiner also disagrees with this statement. Gembitsky et al. teach identifying post-translational modification using a secondary capture agent (page 3, paragraphs 0033, 0034; page 4, paragraphs 0039, 0040; page 5, paragraph 0046; page 7, paragraph 0074). It is also important to note that step five of claim 1, only requires the detection of the presence or absence of the post-translational modification. As was stated in the applicants' response, Gembitsky et al. teaches a method that can indicate that a given whether a protein is modified or not. Thus the reference teaches the instant limitations.

Applicants also put forth arguments addressing the flaws of the Katz and Gembitsky et al.'s methods. However, none of these arguments state that the Katz method combined with the Gembitsky et al.'s method fail to teach the limitations of the instant claims. The Applicants first argue that Katz requires the development of multiple antibodies to discriminate individual post-translational modifications. However, Katz relied upon to teach using a capture agent for the PET, not a capture agent for the post translational modifications. It is unclear how the Applicants arguments address this point.

The Applicants then argue that Gembitsky et al. does not teach digesting the protein and creating peptide fragments. However, the Examiner points out that the instant rejection is made with the combination of two references. Each reference is not required to teach all the limitations of a claim, rather it is the combination of references that must teach all the limitations of a claims. The limitations the applicants are referring to in the arguments against Gembitsky et al. are taught in the Katz reference.

This rejection is maintained from the previous office action and necessitated by amendment.

6. Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katz (US 2002/137119 A1) in view of Gembitsky et al. (US 2005/0153298) further in view of Whaley et al. (Biological Mass Spectrometry, (1991) Volume 20, pages 210-214).

The instant claims are drawn to a method of computationally creating fragments from a sample of proteins and identifying unique proteome epitope tags with a Nearest Neighbor analysis, where each fragment contains a unique proteome epitope tag and obtaining capture agents that selectively binds to the proteome epitope tags.

Katz and Gembitsky et al. are applied as above.

Although Katz teaches computationally analyzing the plurality of fragments according to one parameter defining characteristic of an amino acid sequence (page 2, paragraph 0021) and identifying unique proteome tags (antigens), Katz does not explicitly teach where the parameter is a Nearest Neighbor Analysis that identifies proteome epitope tags.

Regarding claim 4, Whaley et al. teach a method wherein the protein digests (fragments) are analyzed using Nearest Neighbor analysis based on charge (page 212, left column).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Katz and Gembitsky et al. with Whaley et al. to gain the advantage of ranking proteins sequence in order of their importance. Motivation to combine Katz and Gembitsky et al. is provided above. Katz discloses that it is desirable to rank the proteins in accordance to the importance of parameters (page 5, paragraph 0078) to allow the user to identify which sequences have the most desirable traits. However, Katz does not teach a specific method of ranking the proteins sequences. Thus one of ordinary skill in the art would be motivated to find such a ranking system to use in Katz's methods. Nearest Neighbor analysis is a well-known

method of classifying objects in accordance to the user's desired characteristics and with high confidence. Whaley et al. teach applying the Nearest Neighbor analysis to protein fragments. Thus one seeking to use a ranking system for identifying a desired fragment, would seek to use the Nearest Neighbor analysis since it may be applied to protein fragments, as demonstrated by Whaley et al, and since the analysis produces results with a high degree of confidence. Thus it would have been obvious to one of ordinary skill in the art to combine the methods of Katz and Gembitsky et al. with Whaley et al.

Regarding claims 5 and 6, Katz teaches that the capture agents are determined to have the desired high specificity with minimal cross-reactivity (page 4, paragraph 0058; page 7, paragraph 121-123, 130).

This rejection is necessitated by amendment.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Representatives are available to answer your questions daily from 6 am to midnight (EST). When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent

Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199.

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

JL